

Please insert the accompanying paper copy of the Sequence listing, page numbers 1-85, at the end of the application.

REMARKS

Applicants request entry of this amendment in adherence with 37 C.F.R. §§ 1.821-1.825. This amendment is accompanied by a computer disk containing the above named sequences, SEQ ID NOS:1-112, in computer readable form, and a paper copy of the sequence information which has been printed from the computer disk. The sequence listing was inadvertently omitted from the amendment filed on October 1, 2001. Typographical errors have also been corrected.

The information contained in the computer readable disk was prepared through use of the software program "PatentIn" and is identical to that of the paper copy. This amendment contains no new matter.

Attached hereto is a marked-up version of the changes made to the specification by the amendment. The attached page is captioned "VERSION WITH MARKINGS TO SHOW CHANGES MADE."

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 650-326-2400.

Respectfully submitted,



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**VERSION WITH MARKINGS TO SHOW CHANGES MADE**

The paragraph on page 5, line 8, has been amended as follows:

Fig. 2: Oligonucleotides used in vector construction (SEQ ID NOS:111-112).

The paragraph beginning on page 43, line 6, has been amended as follows:

OLIGO #	5' TO 3' SEQUENCE
190	TT ACC CCT GTG GCA AAA GCC GAA GTG CAG CTG GTG GAG TCT GG ( <u>SEQ ID NO:1</u> )
947	TT ACC CCT GTG GCA AAA GCC CAG GTG CAG CTG GTG CAG TCT GG ( <u>SEQ ID NO:2</u> )
949	TT ACC CCT GTG GCA AAA GCC CAG GTG CAG CTG GTG GAG TCT GG ( <u>SEQ ID NO:3</u> )
953	GA TGG GCC CTT GGT GGA GGC ( <u>SEQ ID NO:4</u> )

The paragraph beginning on page 43, line 19, has been amended as follows:

191	CT GCC CAA CCA GCC ATG GCC GAA ATT GTG CTC ACC CAG TCT CC ( <u>SEQ ID NO:5</u> )
938	TC GCT GCC CAA CCA GCC ATG GCC GTC ATC TGG ATG ACC CAG TCT CC ( <u>SEQ ID NO:6</u> )
939	TC GCT GCC CAA CCA GCC ATG GCC AAC ATC CAG ATG ACC CAG TCT CC ( <u>SEQ ID NO:7</u> )
940	TC GCT GCC CAA CCA GCC ATG GCC GCC ATC CGG ATG ACC CAG TCT CC ( <u>SEQ ID NO:8</u> )
941	TC GCT GCC CAA CCA GCC ATG GCC GCC ATC CAG TTG ACC CAG TCT CC ( <u>SEQ ID NO:9</u> )
942	TC GCT GCC CAA CCA GCC ATG GCC GAA ATA GTG ATG ACG CAG TCT CC ( <u>SEQ ID NO:10</u> )
943	TC GCT GCC CAA CCA GCC ATG GCC GAT GTT GTG ATG ACA CAG TCT CC ( <u>SEQ ID NO:11</u> )
944	TC GCT GCC CAA CCA GCC ATG GCC GAA ATT GTG TTG ACG CAG TCT CC ( <u>SEQ ID NO:12</u> )
957	TC GCT GCC CAA CCA GCC ATG GCC GAC ATC CAG ATG ATC CAG TCT CC ( <u>SEQ ID NO:13</u> )

958 TC GCT GCC CAA CCA GCC ATG GCC GAT ATT GTG ATG ACC CAG ACT  
CC (SEQ ID NO:14)  
973 CAG CAG GCA CAC AAC AGA GGC (SEQ ID NO:15)

The paragraph beginning on page 43, line 38, has been amended as follows:

948 TT ACC CCT GTG GCA AAA GCC GAG GTG CAG CTG TTG GAG TCT GG  
(SEQ ID NO:16)  
949 TT ACC CCT GTG GCA AAA GCC GAG GTG CAG CTG GTG CAG TCT GG  
(SEQ ID NO:17)  
947 TT ACC CCT GTG GCA AAA GCC CAG GTG CAG CTA CAG CAG TGG GG  
(SEQ ID NO:18)

The paragraph beginning on page 44, line 38, has been amended as follows:

953 GAC AGA TGG TGC AGC CAC AGT (SEQ ID NO:19)

The paragraph beginning on page 47, line 17, has been amended as follows:

5' ATC TGG CAC ATC ATA TGG ATA AGT TTC GTG TAC AAA ATG CCA GAC CTA GAG  
GAA TTT TAT TTC CAG CTT GGT CCC (SEQ ID NO:20)

The paragraph beginning on page 47, line 22, has been amended as follows:

5' GTG ATG GTG ATG GTG ATG GAT CGG AGT ACC AGG TTA TCG AGC CCT CGA TAT  
TGA GGA GAC GGT GAC TGA (SEQ ID NO:21)

The paragraph beginning on page 47, line 35, has been amended as follows:

Primer 5

5' GCA ACT GTT GGG AAG GG (SEQ ID NO:22)

The paragraph beginning on page 47, line 38, has been amended as follows:

Primer 197

5' TC GCT GCC CAA CCA GCC ATG (SEQ ID NO:23)

The paragraph beginning on page 48, line 8, has been amended as follows:

5' PCR primer (869)- GGG ACC AAG CTG GAA ATA AAA CGG GCT GTG GCT GCA CCA TCT  
GTC T (SEQ ID NO:24)

The paragraph beginning on page 48, line 11, has been amended as follows:

3' PCR primer (870)- ATC TGG CAC ATC ATA TGG ATA AGA CTC TCC CCT GTT GAA GCT  
CTT (SEQ ID NO:25)

The paragraph on page 48, line 14, has been amended as follows:

5' PCR primer (867)- TCA GTC ACC GTC TCC TCA GCC TCC ACC AAG GGC CCA TC  
(SEQ ID NO:26)

The paragraph on page 48, line 16, has been amended as follows:

3' PCR primer (876)- GTG ATG GTG ATG GTG ATG AGA TTT GGG CTC TGC TTT CTT GTC C  
(SEQ ID NO:27)

The paragraph on page 50, line 14, has been amended as follows:

Primer 885

5' TAA GAG CGG TAA GAG TGC CAG (SEQ ID NO:27)

The paragraph beginning on page 64, line 6, has been amended as follows:

The polyclonal IL8 antibody phage form both the 10<sup>9</sup> and 10<sup>10</sup> affinity cuts (see Example 13) were diluted 1/30 in 2 x YT and 1 µl used as template for PCR amplification of the antibody gene inserts with primers 197 (Example 5) and 970 (see below). PCR (3-100 µL reactions) was performed using a high-fidelity PCR system, Expand (Roche Molecular Biochemicals, Indianapolis, IN) to minimize errors incorporated into the DNA product. Each 100 µl reaction contained 100 pmol of 5' primer 197, 100 pmol of 3' primer 970, 0.7 units of Expand DNA polymerase, 10 µl 2 mM dNTPs, 10 µl 10 x Expand reaction buffer, 1 µl diluted phage stock as template, and water to 100 µl. The reaction was carried out in a Perkin-Elmer thermal cycler (Model 9600) using the following thermal profile: one cycle of denaturation at 94 °C (1 min); ten cycles of denaturation (15 sec, 94 °C), annealing (30 sec, 55 °C), elongation (60 sec, 72 °C); fifteen cycles of denaturation (15 sec, 94 °C), annealing (30 sec, 55 °C), elongation (80 sec plus 20 sec for each additional cycle, 72 °C); elongation (6 min, 72 °C); soak (4 °C, indefinitely). The PCR products were ethanol precipitated, pelleted and dried as described above. The DNA was dissolved in water and fractionated by agarose gel electrophoresis. Only full-length products were excised from the gel, purified, and resuspended in water as described earlier.

Primer 970- 5' GT GAT AAA CTA CCG TA AAG CTT ATC GAT GAT AAG CTG  
TCA A TTA GTG ATG GTG ATG GTG ATG AGA TTT G (SEQ ID NO:29)

The paragraph beginning on page 67, line 15, has been amended as follows:

The decapeptide, YPYDVDPDYAS (SEQ ID NO:30), (Chiron Mimotopes Peptide Systems, San Diego, CA) was dissolved (0.3 g) in dry DMF (5.4 mL) in a round bottom flask under argon with moderate stirring. Imidazole (0.02 g) was added to the stirring solution. Separately, acetylthiopropionic acid (0.041 g) was dissolved in 0.55 mL of dry DMF in a round bottom flask with stirring and 0.056 g of 1,1'-carbonyldiimidazole (Aldrich Chemical Co., Milwaukee, WI) was added to the stirring solution. The flask was sealed under argon and stirred for at least 30 min at room temperature. This solution was added to the decapeptide solution and the reaction mixture was stirred for at least six hr at room temperature before the solvent was removed *in vacuo*. The residue in the flask was triturated twice using 10 mL of diethyl ether each time and the ether was decanted. Methylene chloride (20 mL) was added to the residue in the flask and the solid was scraped from the flask and filtered using a fine fritted Buchner funnel. The solid was washed with an additional 20 mL of methylene chloride and the Buchner funnel was dried under vacuum. In order to hydrolyze the derivative to generate a free thiol, it was dissolved in 70% DMF and 1 M potassium hydroxide was added to a final concentration of 0.2 M while mixing vigorously. The derivative solution was allowed to stand for 5 min at room temperature prior to neutralization of the solution by the addition of a solution containing 0.5 M potassium phosphate, 0.1 M borate, pH 7.0, to which concentrated hydrochloric acid has been added to a final concentration of 1 M. The thiol concentration of the hydrolyzed decapeptide derivative was determined by diluting 10  $\mu$ L of the solution into 990  $\mu$ L of a solution containing 0.25 mM 5,5'-dithiobis(2-nitrobenzoic acid) (DTNB, Aldrich Chemical Co., Milwaukee WI) and 0.2 M potassium borate, pH 8.0. The thiol concentration in mM units was equal to the A412(100/13.76).

The paragraph beginning on page 72, line 12, has been amended as follows:

- A- 5' (TCGCTGCCCCAACCAGCCATGGCCAGTGCTAAAGAACTTAGATCTCAG)  
(SEQ ID NO:31)
- B- 5' (GTGATAAACTACCGCATTAAGCTTATCGATGATAAGCTGTCAATTAGTGAT  
GGTGATGGTGATGTGAATTCTCAGCCCTCTTCAA) (SEQ ID NO:32)
- C- 5' (GCAACTCTCTACTGTTTCTCC) (SEQ ID NO:33)
- D- 5' (GAGGATGACGATGAGCGC) (SEQ ID NO:34)

The paragraph on page 75, line 18, has been amended as follows:

M1-1L (SEQ ID NO:35)

The paragraph on page 76, line 4, has been amended as follows:

M1-3L (SEQ ID NO:37)

The paragraph on page 76, line 17, has been amended as follows:

M1-4L (SEQ ID NO:39)

The paragraph on page 76, line 30, has been amended as follows:

M1-5L (SEQ ID NO:41)

The paragraph on page 76, line 43, has been amended as follows:

M1-8L (SEQ ID NO:43)

The paragraph on page 76, line 56, has been amended as follows:

M1-10L (SEQ ID NO:45)

The paragraph on page 77, line 8, has been amended as follows:

M1-21L (SEQ ID NO:47)

The paragraph on page 77, line 19, has been amended as follows:

M1-23L (SEQ ID NO:49)

The paragraph on page 77, line 34, has been amended as follows:

M1-25L (SEQ ID NO:51)

The paragraph on page 77, line 47, has been amended as follows:

M1-1H (SEQ ID NO:53)

The paragraph on page 77, line 60, has been amended as follows:

M1-3H (SEQ ID NO:55)

The paragraph on page 78, line 12, has been amended as follows:

M1-4H (SEQ ID NO:57)

The paragraph on page 78, line 25, has been amended as follows:

M1-5H (SEQ ID NO:59)

The paragraph on page 78, line 38, has been amended as follows:

M1-8H (SEQ ID NO:61)

The paragraph on page 78, line 51, has been amended as follows:

M1-10H (SEQ ID NO:63)

The paragraph on page 79, line 4, has been amended as follows:

M1-21H (SEQ ID NO:65)

The paragraph on page 79, line 17, has been amended as follows:

M1-23H (SEQ ID NO:67)

The paragraph on page 79, line 30, has been amended as follows:

M1-25H (SEQ ID NO:69)

The paragraph on page 79, line 43, has been amended as follows:

M2-11L (SEQ ID NO:71)

The paragraph on page 79, line 56, has been amended as follows:

M2-12L (SEQ ID NO:73)

The paragraph on page 80, line 8, has been amended as follows:

M1-16L (SEQ ID NO:75)

The paragraph on page 80, line 21, has been amended as follows:

M2-18L (SEQ ID NO:77)

The paragraph on page 80, line 34, has been amended as follows:

M2-20L (SEQ ID NO:79)

The paragraph on page 80, line 47, has been amended as follows:

M2-31L (SEQ ID NO:81)

The paragraph on page 80, line 60, has been amended as follows:

M2-32L (SEQ ID NO:83)

The paragraph on page 81, line 12, has been amended as follows:

M2-33L (SEQ ID NO:85)

The paragraph on page 81, line 25, has been amended as follows:

M2-34L (SEQ ID NO:87)

The paragraph on page 81, line 38, has been amended as follows:

M2-35L (SEQ ID NO:89)

The paragraph on page 81, line 51, has been amended as follows:

M2-11H (SEQ ID NO:91)

The paragraph on page 82, line 4, has been amended as follows:

M2-12H (SEQ ID NO:93)

The paragraph on page 82, line 17, has been amended as follows:

M2-16H (SEQ ID NO:95)

The paragraph on page 82, line 30, has been amended as follows:

M2-18H (SEQ ID NO:97)

The paragraph on page 82, line 43, has been amended as follows:

M2-20H (SEQ ID NO:99)

The paragraph on page 82, line 56, has been amended as follows:

M2-31H (SEQ ID NO:101)

The paragraph on page 83, line 8, has been amended as follows:

M2-32H (SEQ ID NO:103)

The paragraph on page 83, line 22, has been amended as follows:

M2-33H (SEQ ID NO:105)

The paragraph on page 83, line 35, has been amended as follows:

M2-34H (SEQ ID NO:107)



The paragraph on page 83, line 48, has been amended as follows:

M2-35H (SEQ ID NO:109)

The paragraph beginning on page 84, line 3, has been amended as follows:

Translated amino acid sequences of sequenced antibodies. M1-H Heavy Chain Variable and CH1 Regions ~~10<sup>-9</sup>M~~ 10<sup>-9</sup>M<sup>-1</sup> Affinity Cut (SEQ ID NOS:64, 54, 66, 68, 70, 56, 58, 60 and 62 respectively)

The paragraph beginning on page 84, line 61, has been amended as follows:

M1-L Kappa Chain Variable and Constant Regions ~~10<sup>-9</sup>M~~ 10<sup>-9</sup>M<sup>-1</sup> Affinity Cut (SEQ ID NOS:46, 36, 48, 50, 52, 38, 40, 42, and 44 respectively)

The paragraph beginning on page 85, line 56, has been amended as follows:

M2-H Heavy Chain VH-CH1 Sequence ~~10<sup>-10</sup>M~~ 10<sup>-10</sup>M<sup>-1</sup> Affinity Cut (SEQ ID NOS:92, 94, 96, 98, 100, 102, 104, 106, 108, and 110 respectively)

The paragraph beginning on page 86, line 57, has been amended as follows:

M2-L Kappa Chain VKCK ~~10<sup>-10</sup>M~~ 10<sup>-10</sup>M<sup>-1</sup> Affinity Cut (Thu Sep 23) (SEQ ID NOS:72, 74, 76, 78, 80, 82, 84, 86, 88, and 90 respectively)